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Two components of the new ESPEN diagnostic criteria for malnutrition are independent predictors of lung function in hospitalized patients with chronic obstructive pulmonary disease (COPD).

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Abstract

Introduction: Low fat free mass index (FFMI) is a component of the ESPEN diagnosis criteria of malnutrition, that only when accompanied with weight loss is considered to be a determinant of malnutrition. Our aims were to assess the prevalence of malnutrition in patients with chronic obstructive pulmonary disease (COPD) applying the ESPEN criteria, and to examine the ability of different components of the criteria to predict COPD severity, length of stay (LOS), hospital readmissions within 30 days and mortality.

Methods: Subjects were COPD patients (n=121) admitted to Landspitali University Hospital from March 2015-March 2016. Patients were screened for nutritional risk using Icelandic screening tool (ISS) and NRS-2002. Body composition was measured by bioelectrical impedance analysis (BIA). Lung function was measured by spirometry.

Results: The prevalence of malnutrition according to the ESPEN criteria was 21%. The association between nutritional assessment, applying different components of the ESPEN criteria, and COPD severity was highly significant, with the highest risk being associated with low FFMI OR (95% CI) 4.77 (2.03, 11.20; p<0.001). There was a trend towards higher risk of hospitalization for >7 days in subjects with low FFMI (OR 2.46 95% CI 0.92, 6.59; p=0.074) and increased risk of 6 and 9 months' mortality (OR 2.72 95% CI 0.88, 8.39, P=0.082 and OR 2.72 95% CI 0.94, 7.87, P=0.065, respectively) in subjects diagnosed as malnourished by the ESPEN criteria.

Conclusion: This study describes the prevalence of malnutrition in hospitalized COPD patients using the ESPEN criteria from 2015. Our findings suggest that FFMI could be used independently of weight loss for the diagnosis of malnutrition in COPD patients, although there remain some problems associated with its measurement in the clinical setting.

Keywords: Malnutrition; COPD; ESPEN malnutrition definition; Nutritional screening

Introduction

For several years screening for nutritional risk has been recommended by national and international societies for clinical nutrition (Kondrup, Allison, et al., 2003) and different tools have been validated during the past decades (Kondrup, Rasmussen, Hamberg, Stanga, & Ad Hoc, 2003; Thorsdottir, Gunnarsdottir, & Eriksen, 2001). Studies have defined a large proportion of patients with chronic obstructive pulmonary disease (COPD) as at nutritional risk, but the prevalence varies (20-45%) depending on which screening tool is used (Collins, Elia, Kurukulaaratchy, & Stratton, 2016; Hogan, Lan, Diep, Gallegos, & Collins, 2016; Thorsdottir et al., 2001; Vermeeren et al., 2006). Most commonly used screening tools rely on assessment of height and body weight, and calculations of body mass index (BMI). Although BMI has been shown to be an independent risk factor in the prognosis of COPD (Schols, Slangen, Volovics, & Wouters, 1998) and overall mortality (Hallin et al., 2007), with increased risk of mortality even in patients with normal BMI compared to those with higher BMI (Cao et al., 2012; Guo et al., 2016), it does not take into account variations in body composition. Age-related loss of muscle, also known as sarcopenia, has been reported in 15% of COPD patients (Jones et al., 2015) and cachexia is a common feature of COPD associated with an increased risk of mortality (Sanders, Kneppers, van de Bool, Langen, & Schols, 2016; von Haehling & Anker, 2014; Wagner, 2008). Therefore, the use of body composition measurements in the assessment of nutritional risk that enable separation of fat mass and the fat free mass components in patients with COPD might be relevant (Gologanu, Ionita, Gartonea, Stanescu, & Bogdan, 2014; Mamoto et al., 2003). A recent statement from the European Society for Clinical Nutrition and Metabolism (ESPEN) based on unanimous consensus of 12 experienced clinical scientists encouraged the development of accessible techniques for body composition measurements in all health care settings (Cederholm

et al., 2015), and proposed new diagnostic criteria for recognition of malnutrition. The definition differs from previous diagnostic criteria as it combines weight loss with either age related BMI or fat free mass index (FFMI) (Cederholm et al., 2015) as a second alternative to low BMI (<18.5 kg/m^2) for diagnosis of malnutrition. Few studies have used these new criteria (Rojer et al., 2016; Sanz-Paris et al., 2016) and none in patients with COPD.

The aims of the present study were to assess the prevalence of malnutrition in patients with chronic obstructive pulmonary disease (COPD) applying the ESPEN criteria, and to examine the ability of different components of the criteria to predict severity of COPD, length of stay (LOS), hospital readmissions within 30 days and mortality.

Materials and Methods

Subjects

Subjects were patients with COPD admitted to the Department of Pulmonary Medicine at Landspitali during one year: March 2015- March 2016 (n=236). The most common reason for admission was exacerbation of COPD. Patients who were judged to be able to maintain balance on a device to measure body composition and had an anticipated length of hospitalization of >3 days (evaluated by medical staff in the department) were invited to participate. Information on height was collected from electronic medical records in Landspitali (SAGA (TM software 3.1.39.9)).

Socio-demographic data, date of admission, readmission within 30 days, LOS and mortality at six and nine months, were collected from electronic medical records SAGA (TM software 3.1.39.9).

Nutritional risk screening

For each patient, nutritional screening was undertaken by a trained researcher on admission using the following screening tools.

Icelandic simple screening (ISS)

This screening tool is recommended by the clinical guidelines for hospital nutrition at Landspitali (Friðriksdóttir, 2011) and was validated against a full nutritional assessment (weight, height, BMI, serum albumin, pre-albumin, lymphocyte count, triceps skinfold thickness, mid-arm muscle circumference, and unintentional weight loss) in COPD patients (Thorsdottir et al., 2001) (appendix 1). Nutritional risk is categorized as low (score 0-1), medium (score 2-3) and high (score ≥ 4). A total score of ≥4 is considered ‘at nutritional risk’.

Nutritional Risk Screening (NRS-2002)

The NRS-2002 screening tool was developed by Danish Society for Parenteral and Enteral Nutrition, recommended by ESPEN and validated using retrospective analysis of 128 randomized controlled trials of nutritional support in different patient groups (Kondrup, Rasmussen, et al., 2003) (appendix 2). Patients are scored in each of two categories according to whether key features are absent (score 0), mild (score 1), moderate (score 2) or severe (score 3), giving a total possible score of 0-6. If patients are ≥ 70 years, 1 point is added to the final score. With a total score of ≥3 a patient is considered 'at nutritional risk'.

ESPEN criteria for the diagnoses of malnutrition

The two alternative ways to diagnose malnutrition proposed by the new ESPEN criteria are summarized in the Fact box. These criteria may be applied after patients have been screened using a validated screening tool to identify those at risk of malnutrition. The data collected on nutritional status and body composition were used to separate patients into groups according to the proposed cut-offs.

Body composition

A portable, multi- frequency (20kHz, 100kHz) bioelectrical impedance analysis (BIA) device (InBody230 Co., Ltd. Korea) was used to measure body composition. The method, based on a low electrical current sent through the body to measure the tissue impedance, has previously been validated in stable COPD patients (Schols, Broekhuizen, Weling-Scheepers, & Wouters, 2005).

The device measures a patient's weight, estimates total body water, fat mass and fat free mass, and calculates BMI. The BIA measurement was performed by the same trained researcher in the

morning, after breakfast within 48 hours from enrolment to the study. FFMI was calculated as fat free mass divided by height squared in kg/m^2 (Schutz, Kyle, & Pichard, 2002).

Classification of disease severity

Forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) were measured by spirometry (Jaeger MS-PFT®, Care Fusion, San Diego, USA) and disease severity was classified using the GOLD criteria (Pauwels et al., 2001). Mild (GOLD 1): $FEV_1 \geq 80$ percent predicted, moderate (GOLD 2): 50 percent $\leq FEV_1 < 80$ percent predicted, severe (GOLD 3): 30 percent $\leq FEV_1 < 50$ percent predicted and very severe (GOLD 4): $FEV_1 < 30$ percent predicted. The measurement was carried out by a trained researcher towards the end of the hospital stay.

Statistical analysis

For statistical analyses IBM SPSS Statistics 24 was used and the level of significance was set at 0.05. The Kolmogorov-Smirnov test was used to test normality of data. Descriptive analyses were presented as means ± SD. Linear regression analyses were used to determine the association between different variables (exposure) related to nutritional assessment: malnutrition according to ESPEN diagnostic criteria, nutritional risk using two validated screening tools (ISS and NRS-2002), each component of the ESPEN diagnostic criteria (unintentional weight loss, age related BMI below cut offs and low FFMI) and disease severity, LOS, six and nine month mortality and 30-day readmission (outcomes). According to policy at Landspitali, the aim is that mean LOS should not exceed 7 days, therefore this was used as the cut-off in our analyses. Adjustments were made for potential confounding variables, such as gender and lung function. Cohen´s kappa (K) was used to determine the agreement between the screening tools (ISS and NRS-2002) and between each screening tool and ESPEN diagnostic criteria for malnutrition.

Kappa is categorized by the strength of agreement as Slight (<0.20), Fair (0.21-0.40), Moderate (0.41-0.60), Substantial (0.61-0.80) and Almost perfect (0.81–1.00) (Viera & Garrett, 2005).

Ethics

The study was approved by the hospital's Bioethics Committee (reference nr. 12/2015) and the medical manager at Landspitali (16, LSH 28-15). Informed written consent was obtained prior to inclusion in the study. If patients were at nutritional risk, appropriate nutritional support was provided e.g. energy- and protein dense food and/or oral nutritional supplement (ONS) and/or dietary advice.

Results

A total of 236 patients were screened for nutritional risk during the study period. Of these, 29 (12%) refused to participate and another 70 (30%) patients were not eligible due to a planned admission of less than three days (n=19). A further forty-two (18%) patients were excluded as they were not able to stand in an upright position for 60 seconds (the time it takes to measure body composition using BIA) or judged by the nursing staff to be too sick to be able to participate. Nine patients were not eligible for other reasons e.g. cognitive impairment. Of those who did not participate in the study, 99 (34%) were defined as at nutritional risk when using the screening tool proposed by Landspitali University hospital (referred to as ISS). Prevalence of nutritional risk in the group defined as not being eligible due to sickness was 18 (43%).

One hundred and thirty-seven patients (58.5%) consented to participate. However, 16 (12%) had insufficient data available (measurement of body composition) e.g. due to admission to the ICU, edema, not able to stand in an upright position for measuring BIA. Data were analysed for 121

167 participants (69 women and 52 men) for whom complete data on screening and body
168 composition was available. A flowchart of recruitment is shown in Figure 1.

169 **Baseline characteristics**

170 Data on anthropometric and functional measurements for all participants included in the final
171 sample (n=121) are shown in Table 1. Data on FEV_1were available for 98 (81%) of the 121
172 subjects and off those, 56 (57%) had severe or very severe disease. Fifty-nine (48%) subjects
173 were classified by BMI as overweight or obese and 36 (30%) had low FFMI.

174 **Prevalence of malnutrition**

175 Nutritional screening using the ISS identified 44 (36%) patients as being at nutritional risk
176 (Table 2). The more widely used screening tool, NRS-2002, identified more patients at
177 nutritional risk than the ISS (n=67 (55%)). Table 2 shows the number (%) of patients who
178 following screening with ISS or NRS-2002 had measurements below the cut-off values
179 suggested by the two alternatives of the ESPEN diagnostic criteria. The number of subjects
180 diagnosed as malnourished was very similar applying the two different screening tools (n=25
181 (21% of all subjects, 57% of those defined as risk by ISS) vs. n=23 (19% of all subjects and
182 34%, of those defined at risk by NRS2002). Applying the ESPEN criteria without screening for
183 nutritional risk first resulted in the same number of subjects diagnosed as malnourished as when
184 applying screening prior to diagnosis, in line with the protocol proposed by ESPEN.

185 A moderate agreement between the two screening tools used in our study was seen by Cohen's
186 kappa analysis ($K=0.470$, $p < 0.001$). Substantial agreement was seen between the ISS and the
187 ESPEN criteria of malnutrition ($K=0.626$, $p < 0.001$) while the agreement between NRS-2002
188 and the ESPEN criteria of malnutrition was fair ($K=0.285$, $p < 0.001$).

Eight subjects who were found to have a low FFMI were not considered to be at nutritional risk by screening. These subjects did not report weight loss in the past months and had a significantly higher BMI than subjects with low FFMI defined at nutritional risk (23.5±2.6 vs. 17.9±2.0, p<0.001) (supplemental table 4).

Outcomes

COPD severity

The association between nutritional status (defined by two different screening tools and each alternative of the ESPEN criteria) and severity of COPD was highly significant, with low FFMI being the variable associated with the highest risk of being at a severe or very severe stage of the disease (OR 4.77 95% CI 2.03, 11.20; p<0.001) (Table 3). Unintentional weight loss was not found to be associated with severity of COPD in our study.

Length of stay and readmissions

Higher risk of prolonged hospitalization (>7 days) was seen in subjects with low FFMI (OR 2.46 95% CI 0.92, 6.59; p=0.074), although the results were not statistically significant (Table 3). No associations were found between each alternative of the ESPEN diagnosis for malnutrition or nutritional risk by the ISS or NRS-2002 and readmission within 30 days.

Mortality

Being defined as at nutritional risk by the Icelandic screening sheet (ISS) was found to predict mortality within 6 and 9 months from admission to the hospital (OR 3.48 95% CI 1.12, 10.37, P=0.025 and OR 2.88 95% CI 1.06, 7.82, P=0.039, respectively). Unintentional weight loss also independently predicted mortality 6 months after hospitalization (OR 3.88 95% CI 1.14, 13.26, P=0.030). However, these associations did not remain statistically significant after adjusting for

lung function. Being defined at nutritional risk by NRS-2002 was not associated with increased risk of mortality, while a trend towards increased risk was observed among those diagnosed malnourished by ESPEN criteria.

Discussion

The present study describes the prevalence of malnutrition in hospitalized COPD patients according to the new ESPEN diagnostic criteria for malnutrition. Twenty-five (21%) of patients were categorized as malnourished, although interestingly, in our study sample, use of nutritional screening prior to applying the ESPEN criteria did not result in recognition of any more patients than applying the ESPEN criteria directly without the screening step. Eight subjects (1%) were found to have low FFMI but were not considered to be at nutritional risk by screening. This raises questions about whether FFMI should be part of nutritional screening which is often undertaken by staff with fewer skills in nutritional assessment. Despite the limited data set used in nutritional screening there are often difficulties in getting screening completed reliably in many places. If low FFMI is indicative of nutritional risk in the absence of change in the other parameters of nutritional screening, this raises questions about the skills needed in those conducting screening. On average, this group had a higher BMI than subjects with low FFMI defined at nutritional risk by nutritional screening (23.5±2.6 vs. 17.9±2.0, $p<0.001$). It has been shown that even patients with a normal BMI have increased risk of mortality compared to those with higher BMI (Cao et al., 2012; Guo et al., 2016). The use of such low BMI cut-off (<18.5 kg/m^2) as suggested in the ESPEN diagnostic criteria in a disease characterized by wasting might not be suitable. In our study, patients with low FFMI (<15 and 17 kg/m^2 in women and men, respectively) but not identified as at nutritional risk had a mean BMI of 23.5 kg/m^2 but the

number of patients was small and further studies are needed to investigate this in the COPD population.

In our study, we found a strong association between FFMI and severity of COPD. Previous studies have reported low FFMI as a useful predictor of disease severity and mortality (Luo et al., 2016; Schols et al., 2005; Slinde, Gronberg, Engstrom, Rossander-Hulthen, & Larsson, 2005). Our results and reports from other studies raises the question as to whether FFMI should be used as an independent criterion for diagnosis of malnutrition in COPD as changes in body compositions can occur well before any weight loss (Schols et al., 1998) In our study, using FFMI independently would have resulted in eight additional patients recognized as malnourished using the ESPEN criteria, and without measuring FFMI it is likely that some patients with normal or even high BMI would go undetected despite being muscle depleted (Vermeeren et al., 2006).

The aetiology of malnutrition in COPD is complex and it is difficult to determine whether FFM depletion results from changes to nutritional status or to disease processes which might have implications for the nutritional management of patients. Inflammation is a reaction to many diseases, including COPD, which can lead to substantial loss of FFM. If inflammation markers like C-reactive protein (CRP) and transthyretin (pre-albumin) are not taken into account in the diagnosis of malnutrition it is hard to prioritize treatment and to know if any potential benefits are from the nutritional therapy or other medical treatment (Soeters et al., 2016). However, successful dietary intervention in this patient group, have been demonstrated, with low quality evidence from RCTs mainly in patients with stable COPD of improvements in FFM, suggesting that nutritional depletion is not entirely an epiphenomenon of the disease (Ferreira, Brooks, White, & Goldstein, 2012).

In some recent studies using the new ESPEN criteria information on FFMI is lacking (Poulia et al., 2016; Sanz-Paris et al., 2016). It is a limitation of the current study that BIA is not the gold standard method for measuring body composition and not validated in hospitalized patients who sometimes may have fluid disturbance. However, BIA is quick and inexpensive compared to many other methods and in the ESPEN consensus statement (Cederholm et al., 2015) the use of any technical devices like BIA are approved for measuring FFM. Another limitation to the BIA method used in this study is that it depends on the ability to stand for 60 seconds. In our study, 42 patients (18% of the total number of patients recruited to the hospital in the study period) were excluded from participation as they were not stable enough to stand on the device. A different device would therefore be required if measurements of FFMI were to be used in routine clinical practice.

The two screening tools used in the present study were developed with quite similiar aims in mind. The Icelandic tool was validated in COPD patients with the aim of identifying patients that require further nutritional assessment and treatment, and the NRS-2002 was designed to identify hospitalized patients likely to benefit from nutritional support not only to find those who are likely to be at nutritional risk. However, there are some differences between the two tools which may explain the large difference in the proportion of patients found to be at nutritional risk in this study. For example, the NRS-2002 adds 1 point to the score for having COPD, therefore all of our subjects received this point. Another difference is that the question; *"Has the patient been hospitalised for 5 days or more during previous 2 months*?" is included in the ISS but not in NRS-2002, which might partly explain the association seen between nutritional risk by ISS and mortality in the present study. Interestingly, NRS-2002 failed to recognize 2 patients, identified by ISS at nutritional risk and ESPEN as malnourished. Again, there is some difference between

279 the tools and criteria used. For example, low BMI (<18.5 kg/m^2) was seen in one of those
280 patients. By using ISS that criteria alone gave him 4 points, which is the cut-off for being at
281 nutritional risk, and he was diagnosed as malnourished by ESPEN (Fact box, alternative 1).
282 However, by using NRS-2002 he only was allocated only 1 point for the low BMI and 1 point
283 for COPD, giving him a total score of 2 points (≥3 is considered at nutritional risk). Although
284 many tools have been developed and implemented in different patient groups, there is no
285 consensus on which tool is the most optimal. Recent meta-analysis concluded that it´s more
286 important to do the screening for nutritional risk than the screening tool itself (van Bokhorst-de
287 van der Schueren, Guaitoli, Jansma, & de Vet, 2014).

288 One of the strengths of our study is that the study population is well defined i.e. hospitalised
289 patients with COPD. However, a relatively small sample size is a limiting factor. Although,
290 statistically significant associations with being 'at nutritional risk' or being malnourished were
291 found for only a few of the outcomes assessed in our study, we cannot rule out associations
292 previously seen in other studies. In our study, unintentional weight loss was the only component
293 of the ESPEN criteria significantly associated with increased risk of mortality, although the
294 association did not remain significant after adjustment. Unintentional weight loss has previously
295 been associated with higher mortality in patients with COPD (Prescott et al., 2002).

296 Our study describes the prevalence of malnutrition in hospitalized patients with COPD using the
297 ESPEN criteria proposed in 2015. Our findings suggest that FFMI could be used independently
298 of weight loss for the diagnosis of malnutrition in COPD patients, although there remain some
299 problems associated with its measurement in the clinical setting.

300

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Statement of authorship

Concept and design of study and finalizing manuscript; ARI, IG, AMB, CB, CEW, AR, TG and OGG. Data collection and data management; ARI. Analyzing and interpretation of data; ARI, IG, AMB, CB, CEW, AR, TG and OGG. Writing the manuscript; ARI. All authors participated in editing and final revisions of the manuscript. All authors have read and approved the final manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

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411 **Figure and Table Legends**

412 **Appendix 1**

NATIONAL UNIVERSITY HOSPITAL
Department of Clinical Nutrition **SCREENING FOR MALNUTRITION**

This screening sheet should be used to assess adult patients' need for nutritional therapy.

Answer the following questions and assess scores accordingly. If the sum of a patient's scores is 5 or more, a referral should be sent to the Department of Clinical Nutrition.

PATIENT'S I.D.

QUESTION	ANSWER	ASSESSMENT	SCORES
1. Height:_____m Weight:_____kg	BMI: Kg/m_ _____	>20 0 points 18-20: 2 points < 18: 4 points	_____
2. Recent unintentional weight loss? ☐ Yes ☐ No If yes, how much? _____kg Over what period? _____months	% of weight loss _____	Unintentional weight loss: >5% past month or > 10 % previous 6 mo. 4 points 5-10% " 1-6 mo. 2 points Other 0 points	_____
		Question 3 to 8: Yes: 1 point No: 0 points	
3. Is patient over age 65? ☐ Yes ☐ No			_____
4. Problems last weeks or months?			
A. Vomiting lasting more than 3 days ? ☐ Yes ☐ No			_____
B. Daily diarrhoea (more than 3 liquid stools per day)? ☐ Yes ☐ No			_____
C. Continuous loss of appetite or nausea? ☐ Yes ☐ No			_____
D. Difficulty in chewing or swallowing? ☐ Yes ☐ No			
5. Hospitalised for 5 days or more during previous 2 months? ☐ Yes ☐ No			_____
6. Major surgery in the past month? ☐ Yes ☐ No If yes, list type _____			_____
7. Diseases – 5 points ☐ Yes ☐ No Burn >15 % Malnutrition Multiple trauma			_____

Completed by_____ Date_____ **Sum scores** _____
signature

415 **Appendix 2**

Nutritional Risk Screening (NRS 2002)

Table 1 Initial screening			
		Yes	No
1	Is BMI <20.5?		
2	Has the patient lost weight within the last 3 months?		
3	Has the patient had a reduced dietary intake in the last week?		
4	Is the patient severely ill ? (e.g. in intensive therapy)		
Yes: If the answer is 'Yes' to any question, the screening in Table 2 is performed. **No**: If the answer is 'No' to all questions, the patient is re-screened at weekly intervals. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

Table 2 Final screening			
Impaired nutritional status		**Severity of disease (≈ increase in requirements)**	
Absent **Score 0**	Normal nutritional status	Absent **Score 0**	Normal nutritional requirements
Mild **Score 1**	Wt loss >5% in 3 mths or Food intake below 50–75% of normal requirement in preceding week	Mild **Score 1**	Hip fracture• Chronic patients, in particular with acute complications: cirrhosis•, COPD•. *Chronic hemodialysis, diabetes, oncology*
Moderate **Score 2**	Wt loss >5% in 2 mths or BMI 18.5 – 20.5 + impaired general condition or Food intake 25–60% of normal requirement in preceding week	Moderate **Score 2**	Major abdominal surgery• Stroke• *Severe pneumonia, hematologic malignancy*
Severe **Score 3**	Wt loss >5% in 1 mth (>15% in 3 mths) or BMI <18.5 + impaired general condition or Food intake 0-25% of normal requirement in preceding week in preceding week.	Severe **Score 3**	Head injury• Bone marrow transplantation• *Intensive care patients (APACHE>10).*
Score:	+	**Score:**	**= Total score**
Age	if ≥70 years: add 1 to total score above	**= age-adjusted total score**	
Score ≥3: the patient is nutritionally at-risk and a nutritional care plan is initiated **Score <3**: weekly rescreening of the patient. If the patient e.g. is scheduled for a major operation, a preventive nutritional care plan is considered to avoid the associated risk status.			

NRS-2002 is based on an interpre-tation of available randomized clinical trials.
•indicates that a trial directly supports the categorization of patients with that diagnosis. Diagnoses shown in *italics* are based on the prototypes given below.
Nutritional risk is defined by the present **nutritional status** and risk of impairment of present status, due to **increased requirements** caused by stress metabolism of the clinical condition.

A nutritional care plan is indicated in all patients who are

(1) severely undernourished (score = 3), or (2) severely ill (score = 3), or (3) moderately undernourished + mildly ill (score 2 +1), or (4) mildly undernourished + moderately ill (score 1 + 2).

Prototypes for severity of disease
Score = 1: a patient with chronic disease, admitted to hospital due to complications. The patient is weak but out of bed regularly. Protein requirement is increased, but can be covered by oral diet or supplements in most cases.

Score = 2: a patient confined to bed due to illness, e.g. following major abdominal surgery. Protein requirement is substantially increased, but can be covered, although artificial feeding is required in many cases.

Score = 3: a patient in intensive care with assisted ventilation etc. Protein requirement is increased and cannot be covered even by artificial feeding. Protein breakdown and nitrogen loss can be significantly attenuated.

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Fact box

The ESPEN diagnosis of malnutrition may be applied after patients have been screened using a validated screening tool to identify those at nutritional risk

Alternative 1:

- BMI < 18.5 kg/m^2

Alternative 2:

- Weight loss (Unintentional) >10% indefinite of time, or >5% over the last 3 months combined with either

- BMI <20 kg/m^2 if <70 years of age, or <22 kg/m^2 if ≥70 years of age or

- FFMI <15 and 17 kg/m^2 in women and men, respectively

Table 1. Baseline characteristics

	N=121
Age (years), mean (SD)	73.7 (9.0)
Gender	
Male, n (%)	52 (43)
Female, n (%)	69 (57)
Height (cm), mean (SD)	168.2 (9.4)
Weight (kg), mean (SD)	72.7 (20.5)
Weight loss, n (%)[*]	16 (13)
>10% indefinite of time	13 (81)
>5% over the last 3 months	3 (19)
Body mass index (kg/m^2), mean (SD)	25.7 (6.7)
<18.5 kg/m^2, n (%)	19 (16)
18.5-24.9 kg/m^2, n (%)	43 (36)
25.0-29.9 kg/m^2, n (%)	26 (21)
>30.0 kg/m^2, n (%)	33 (27)
Body fat mass (kg), mean (SD)	22.4 (14.0)
Fat free mass (kg), mean (SD)	50.4 (12.0)
Fat free mass index (kg/m^2), mean (SD)	17.7 (3.3)
Low FFMI, n (%)[†]	36 (30)
FFMI <15 female, n (%)	20 (56)
FFMI <17 male, n (%)	16 (44)
FEV_1 (% of predicted), mean (SD)[‡]	45.7 (20.9)
Gold stage	
Stage I (mild), n (%)	7 (7)
Stage II (moderate), n (%)	35 (36)
Stage III (severe), n (%)	35 (36)
Stage IV (very severe), n (%)	21 (21)

[*] Unintentional weight loss >10% indefinite of time, or >5% over the last 3 months
[†] FFMI < 15 for female and < 17 for male
[‡] n=98

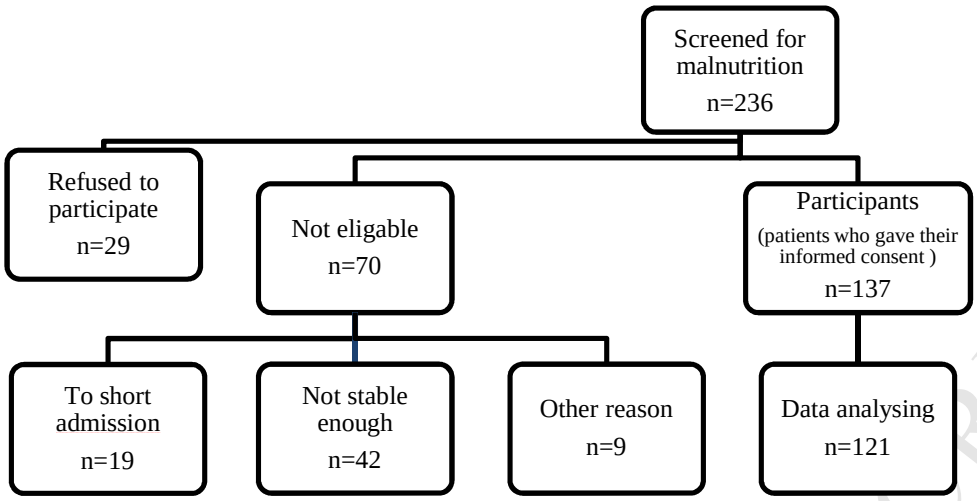

Figure 1 Study flow chart

Table 2. The number of patients being at risk of malnutrition by two screening tools and diagnosed as malnourished according to the new ESPEN criteria

	At risk (ISS)[§] n=44	**At risk (NRS-2002)[**] n=67**	**Malnourished (ESPEN)[††] n=25**
Age (years), mean (SD)	76.0 (8.9)	75.8 (9.1)	74.8 (9.3)
Gender			
Male, n (%)	19 (43)	30 (45)	12 (48)
Female, n (%)	25 (57)	37 (55)	13 (52)
Height (cm), mean (SD)	168.0 (11.1)	169.2 (10.5)	170.0 (9.5)
Weight (kg), mean (SD)	56.9 (14.2)	67.0 (19.0)	51.2 (8.1)
Weight loss, n (%)[‡‡]	16 (36)	15 (22)	10 (40)
Body mass index (kg/m^2), mean (SD)	20.1 (4.6)	23.3 (6.2)	17.7 (1.9)
<18.5 kg/m^2, n (%)	19 (43)	18 (27)	19 (76)
18.5-24.9 kg/m^2, n (%)	20 (46)	25 (37)	6 (24)
25.0-29.9 kg/m^2, n (%)	4 (9)	15 (22)	0 (0)
>30.0 kg/m^2, n (%)	1 (2)	9 (13)	0 (0)
Body fat mass (kg), mean (SD)	12.6 (9.0)	18.7 (12.7)	9.2 (4.5)
Fat free mass (kg), mean (SD)	44.3 (10.8)	48.3 (11.4)	42.0 (8.2)
Fat free mass index (kg/m^2), mean (SD)	15.6 (2.9)	16.7 (2.9)	14.4 (1.6)
Low FFMI, n (%)[§§]	28 (64)	28 (42)	21 (84)
FFMI <15 female, n (%)	15 (54)	15 (54)	10 (48)
FFMI <17 male, n (%)	13 (46)	13 (46)	11 (52)
FEV_1 (% of predicted), mean (SD)[***]	40.3 (17.5)	42.6 (19.2)	35.2 (12.2)
Gold stage			
Stage I (mild), n (%)	1 (3)	3 (5)	0 (0)
Stage II (moderate), n (%)	8 (23)	18 (31)	2 (11)
Stage III (severe), n (%)	18 (51)	26 (44)	11 (58)
Stage IV (very severe), n (%)	8 (23)	12 (20)	6 (32)
ESPEN proposed diagnostic criteria			
Alternative 1			
BMI < 18.5 kg/m^2, n (%)	19 (43)	18 (27)	19 (76)
Alternative 2			
Weight loss (unintentional) + low BMI, n (%)	9 (20)	9 (13)	9 (36)
Weight loss (unintentional) + low FFMI, n (%)	7 (16)	6 (9)	7 (28)
Total number of subjects diagnosed malnourished when applying alternative 1 and/or 2, n (%)	25 (57)	23 (34)	25 (100)

[§] Icelandic screening sheet (ISS). At risk: score of ≥ 4, not at risk: score of ≤ 3
[**] Nutritional risk screening (NRS-2002). At risk: score of ≥ 3, not at risk: score of ≤ 2
[††] Screened at nutritional risk using ISS before applying the ESPEN criteria
[‡‡] Unintentional weight loss >10% indefinite of time, or >5% over the last 3 months
[§§] FFMI < 15 for female and < 17 for male
[***] At risk (ISS) n=35, At risk (NRS-2002) n=59, Malnourished (ESPEN) n=19

Table 3. Linear regression analyses of nutritional risk assessed by two screening tools and malnutrition diagnose according to ESPEN new criteria, and COPD severity, length of stay > 7 days, 30-day readmission and mortality at 6 and 9 months. Unadjusted and adjusted results.

Severe or very severe stage of disease (chronic obstructive pulmonary disease)[j]

		Model 1[k]			Model 2[l]			
	n	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**	
At risk (ISS)	35	2.263	1.063	4.818	0.034	2.264	1.063	4.822	0.034
At risk (NRS-2002)	59	2.621	1.245	5.515	0.011	2.612	1.241	5.500	0.011
Malnourished (ESPEN)	19	3.106	1.221	7.902	0.017	3.091	1.214	7.871	0.018
Unintentional weight loss	12	0.889	0.308	2.564	0.828	0.888	0.308	2.563	0.826
Low age related BMI	31	3.226	1.443	7.210	0.004	3.217	1.435	7.216	0.005
Low FFMI	30	4.767	2.029	11.200	<0.001	4.761	2.026	11.190	<0.001

Length of stay (LOS) more than 7 days

		Model 1[l]			Model 2[m]			Model 3[m]			
	n	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**	
At risk (ISS)	44	1.870	0.780	4.481	0.161	1.936	0.787	4.763	0.150	2.020	0.722	5.655	0.181
At risk (NRS-2002)	67	1.594	0.718	3.537	0.252	1.566	0.688	3.564	0.285	1.637	0.646	4.145	0.299
Malnourished (ESPEN)	25	2.386	0.753	7.560	0.139	2.326	0.715	7.562	0.160	1.573	0.444	5.571	0.482
Unintentional weight loss	16	0.839	0.268	2.626	0.743	0.821	0.252	2.671	0.743	0.730	0.194	2.748	0.642
Low age related BMI	38	2.135	0.834	5.466	0.114	1.983	0.756	5.200	0.164	2.013	0.686	5.910	0.203
Low FFMI	36	2.456	0.916	6.586	0.074	2.525	0.918	6.943	0.073	1.966	0.635	6.086	0.241

OR: Odd ratio, CI: confidence interval

[j] Severe stage: 30 percent ≤ FEV_1 <50 percent predicted. Very severe: FEV_1 <30 percent predicted

[k] Unadjusted

[l] Adjusted for sex

[n] Adjusted for sex and lung function

Readmission within 30 days												
		Model 1[l]			**Model 2[m]**				**Model 3[n]**			
	n	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**
At risk (ISS)	44	1.216	0.493	2.999	0.672	1.216	0.493	2.998	0.672	0.974	0.319	2.974	0.963
At risk (NRS-2002)	67	1.955	0.771	4.959	0.158	1.953	0.769	4.957	0.159	1.767	0.559	5,585	0.332
Malnourished (ESPEN)	25	0.950	0.317	2.845	0.927	0.947	0.316	2.839	0.922	0.483	0.097	2.400	0.374
Unintentional weight loss	16	2.716	0.879	8.386	0.082	2.715	0.879	8.384	0.083	1.706	0.407	7.143	0.465
Low age related BMI	38	0.815	0.308	2.156	0.681	0.809	0.305	2.150	0.671	0.511	0.144	1.819	0.300
Low FFMI	36	1.437	0.567	3.643	0.444	1.436	0.567	3.641	0.446	1.133	0.342	3.758	0.838
Mortality within 6 months												
		Model 1[l]			**Model 2[m]**				**Model 3[n]**			
	n	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**
At risk (ISS)	44	3.480	1.168	10.368	0.025	3.528	1.175	10.590	0.025	2.744	0.731	10.303	0.135
At risk (NRS-2002)	67	1.925	0.625	5.926	0.254	1.890	0.611	5.851	0.269	1.835	0.467	7.208	0.384
Malnourished (ESPEN)	25	2.716	0.879	8.386	0.082	2.646	0.850	8.234	0.093	1.169	0.209	6.526	0.859
Unintentional weight loss	16	3.884	1.138	13.260	0.030	3.945	1.141	13.647	0.030	1.747	0.319	9.560	0.520
Low age related BMI	38	1.857	0.635	5.429	0.258	1.761	0.597	5.197	0.305	1.685	0.411	6.904	0.469
Low FFMI	36	2.038	0.695	5.981	0.195	2.029	0.687	5.993	0.200	1.591	0.390	6.491	0.517
Mortality within 9 months												
		Model 1[l]			**Model 2[m]**				**Model 3[n]**			
	n	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**	**OR**	**95% CI**		**P-value**
At risk (ISS)	44	2.875	1.057	7.821	0.039	2.895	1.059	7.909	0.038	1.888	0.550	6.476	0.312
At risk (NRS-2002)	67	1.465	0.533	4.023	0.459	1.442	0.523	3.974	0.479	1.077	0.321	3.621	0.904
Malnourished (ESPEN)	25	2.722	0.941	7.874	0.065	2.668	0.918	7.752	0.071	0.917	0.171	4.931	0.920
Unintentional weight loss	16	2.955	0.892	9.785	0.076	2.971	0.891	9.909	0.076	1.394	0.261	7.438	0.697
Low age related BMI	38	1.745	0.639	4.770	0.278	1.677	0.609	4.616	0.317	1.230	0.320	4.730	0.763
Low FFMI	36	1.922	0.701	5.273	0.204	1.913	0.694	5.268	0.210	1.197	0.309	4.636	0.795

OR: Odd ratio, CI: confidence interval
[l] Unadjusted
[m] Adjusted for sex
[n] Adjusted for sex and lung function

Supplemental table 4:

Table 4. Main characteristics in patients with low FFMI[n]

	Not at nutritional risk n=8	At nutritional risk[o] n=28	P-value
Age (years), mean (SD)	70.3 (10.5)	76.3 (8.9)	0.111
Gender			
Male, n (%)	3 (38)	13 (46)	
Female, n (%)	5 (62)	15 (54)	
Height (cm), mean (SD)	169.9 (8.4)	167.6 (10.0)	0.558
Weight (kg), mean (SD)	67.6 (6.7)	50.4 (7.2)	<0.001
Weight loss, n (%)[p]	0 (0)	7 (25)	
Body mass index (kg/m^2), mean (SD)	23.5 (2.6)	17.9 (2.0)	<0.001
<18.5 kg/m^2, n (%)	0 (0)	18 (64)	
18.5-24.9 kg/m^2, n (%)	6 (75)	10 (36)	
25.0-29.9 kg/m^2, n (%)	2 (25)	0 (0)	
>30.0 kg/m^2, n (%)	0 (0)	0 (0)	
Body fat mass (kg), mean (SD)	23.3 (6.1)	10.9 (5.5)	<0.001
Fat free mass (kg), mean (SD)	44.3 (6.6)	39.5 (7.4)	0.106
Fat free mass index (kg/m^2), mean (SD)	15.3 (1.1)	13.9 (1.4)	0.016
FEV1 (% of predicted), mean (SD)[q]	37.3 (38.4)	35.1 (15.1)	0.824
Gold stage			
Stage I (mild), n (%)	1 (14)	0 (0)	
Stage II (moderate), n (%)	0 (0)	3 (13)	
Stage III (severe), n (%)	2 (29)	13 (57)	
Stage IV (very severe), n (%)	4 (57)	7 (30)	

[n] FFMI < 15 for female and < 17 for male
[o] At risk: score of ≥ 4, not at risk: score of ≤ 3
[p] Unintentional weight loss >10% indefinite of time, or >5% over the last 3 months
[q] Not at nutritional risk n=7, at nutritional risk n=23